

H36.D2.B7 ANTI-TISSUE FACTOR LIGHT CHAIN VARIABLE REGION

GACATTCAGATGACCCAGTCTCCTGCCTCCAGTCTGCATCTCTGGGAGAAAGTGTCAACCATCACATGC  
D I Q M T Q S P A S Q S A S L G E S V T I T C

CTGGCAAGTCAGACCAATTGATACATGGTTAGCATGGTATCAGCAGAAACCAGGAAATCTCCTCAGCTC  
L A S Q T I D T W L A W Y Q Q K P G K S P Q L

CTGATTATGCTGCCACCAACTTGGCAGATGGGTCCCATCAAGTTTCAGTGGCAGTGGATCTGGCACA  
L I Y A A T N L A D G V P S R F S G S G S G T

AAATTTTCTTTCAAGATCAGCAGCCTACAGGCTGAAGATTTTGTAATATT TACTGTCAACAAGTTTAC  
K F S F K I S S L Q A E D F V N Y Y C Q Q V Y

AGTTCCTCATTACGTTTCGGTGCTGGGACCAAGCTGGAGCTGAAA  
S S P F T F G A G T K L E L K

FIG. 1A

H36.D2.B7 ANTI-TISSUE FACTOR HEAVY CHAIN VARIABLE REGION

GAGATCCAGCTGCAGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGCAGGTATCCTGCAAG  
E I Q L Q Q S G P E L V K P G A S V Q V S C K

ACTTCTGGTTACTCATTGACTACAAACGTTGACTGGGTGAGGCAGAGCCCATGGAAAGAGCCCTTGAG  
T S G Y S F T D Y N V Y W V R Q S H G K S L E

TGGATTGGATAATTTGATCCTTACAAITGGTATTACTATCTACGACCAGAACTTCAAGGGCAAGGCCACA  
W I G Y I D P Y N G I T I Y D Q N F K G K A T

TTGACTGTTGACAAAGTCTTCCACACAGCCTTCATGCATCTCAACAGCCTGACATCTGACGACTCTGCA  
L T V D K S S T T A F M H L N S L T S D D S A

GTTTATTTCTGTGCAAGAGATGTGACTACGGCCCTTGACTTCTGGGGCCAAGGCACCACTCTCACAGTC  
V Y F C A R D V T T A L D F W G Q G T T L T V

TCCTCA  
S S

FIG. 1B

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ANTIBODY	APPARENT $K_1$ , M <sup>-1</sup>	APPARENT $K_1$ , M
BY ELISA		
D2	$5.2 \times 10^9$	$1.9 \times 10^{-10}$
I47	$6.5 \times 10^9$	$1.5 \times 10^{-10}$
K73	$9.8 \times 10^9$	$1.0 \times 10^{-10}$
K80	$2.3 \times 10^9$	$4.3 \times 10^{-10}$
L102	$2.5 \times 10^9$	$4.0 \times 10^{-10}$
L133	$1.7 \times 10^9$	$5.9 \times 10^{-10}$
BY BIACore		
H36	$3.1 \times 10^{10}$	$3.2 \times 10^{-11}$
I43	$2.3 \times 10^9$	$4.3 \times 10^{-10}$
I47	$3.2 \times 10^9$	$3.1 \times 10^{-10}$
L133	$4.6 \times 10^9$	$2.2 \times 10^{-10}$
M107	$1.1 \times 10^9$	$9.1 \times 10^{-10}$

FIG. 2

ANTIBODY NAME	% INHIBITION ANTIBODY PREINCUBATED WITH TF/VIIa
D1	0
D1B	1
H31	4
H36	95
I43	1
J131	7
K80	0
K82	0
K87	1
L97B	7
L101	0
L102	0
L105	0
L133	0
M5	1
M107	34

FIG. 3

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ANTIBODY NAME	<u>% INHIBITION</u> TF PREINCUBATED WITH ANTIBODY PRIOR TO ADDITION OF VIIa	<u>% INHIBITION</u> TF PREINCUBATED WITH VIIa PRIOR TO ADDITION OF ANTIBODY
D1	15	nd
D1B	48	12.7
H31	64	21
H36	0	0
I43	68	55
J131	38	11
K80	12	nd
K82	0	nd
K87	0	nd
L96	0	nd
L101	38	11
L102	14	nd
L105	4	nd
L133	13	nd
M5	0	nd
M107	0	nd

FIG. 4

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[rhTF], nM	[H36.D2], nM	H36.D2/rhTF MOLAR RATIO	CLOTTING TIME (SECONDS)	% INHIBITION OF rhTF FUNCTION
0.0048	0	0	102.3	0
	1.61	335.4	114.3	31.3
	3.23	670.8	121.3	45.8
0.023	0	0	77.6	0
	1.61	70.0	85.3	52.2
	3.23	140.0	91.1	65.2
	6.45	280.4	99.6	73.9
0.092	0	0	49.3	0
	3.23	35.1	65.8	65.2
	6.45	70.1	88.5	90.2
	12.90	140.2	113.3	95.7
0.46	0	0	32.6	0
	6.45	14.0	52.7	82.4
	12.90	28.0	80.2	96.7
	32.30	70.2	117.9	99.3
2.30	0	0	23.9	0
	16.10	7.0	47.1	94.4
	32.30	14.0	95.2	99.7
	64.50	28.0	115.3	99.9
11.52	0	0	22.2	0
	16.10	1.4	30.2	93.4
	32.30	2.8	46.0	98.8
	64.50	5.6	87.6	99.9
	161.30	14.0	114.0	100.0

FIG. 5

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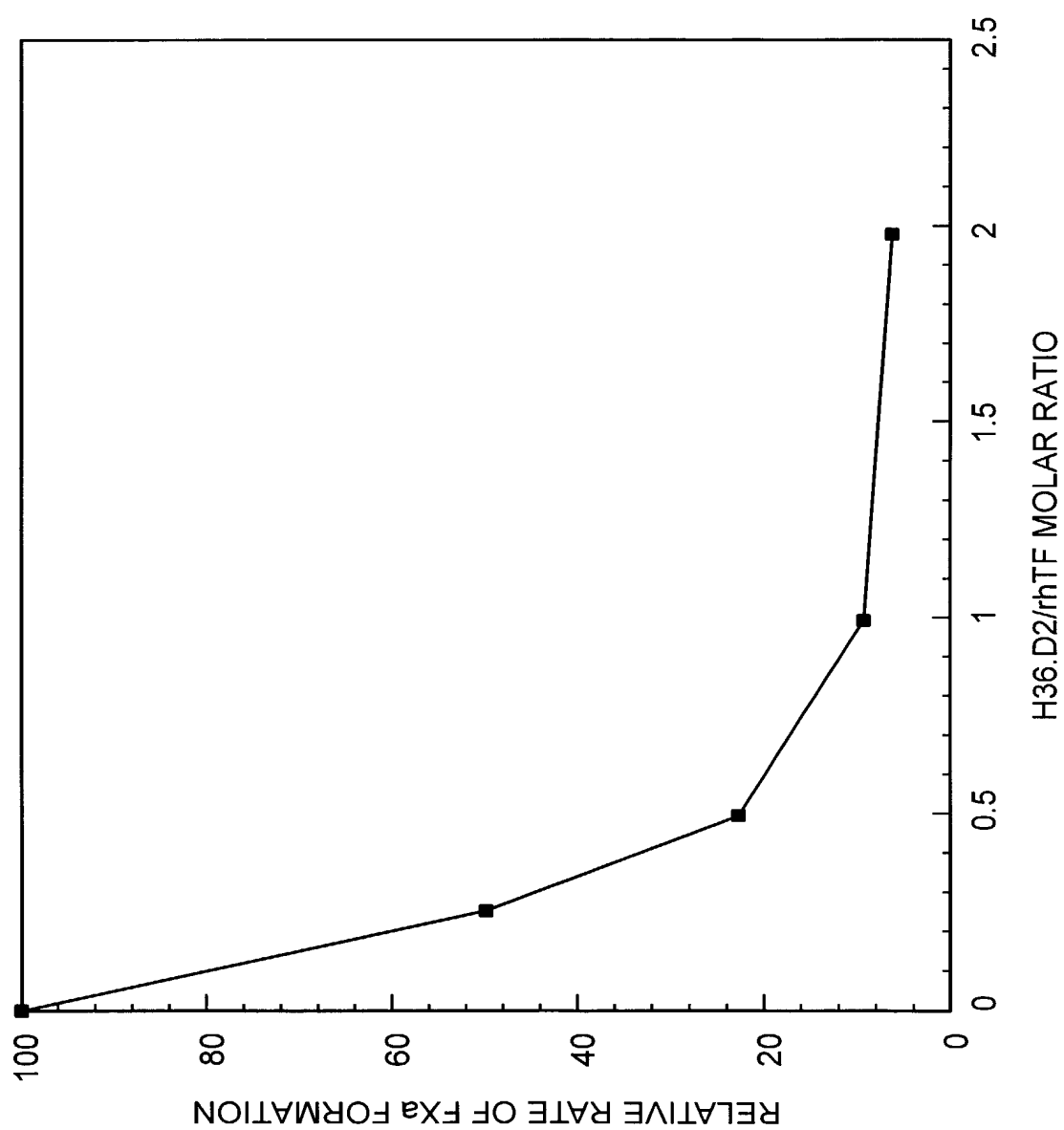


FIG. 6A

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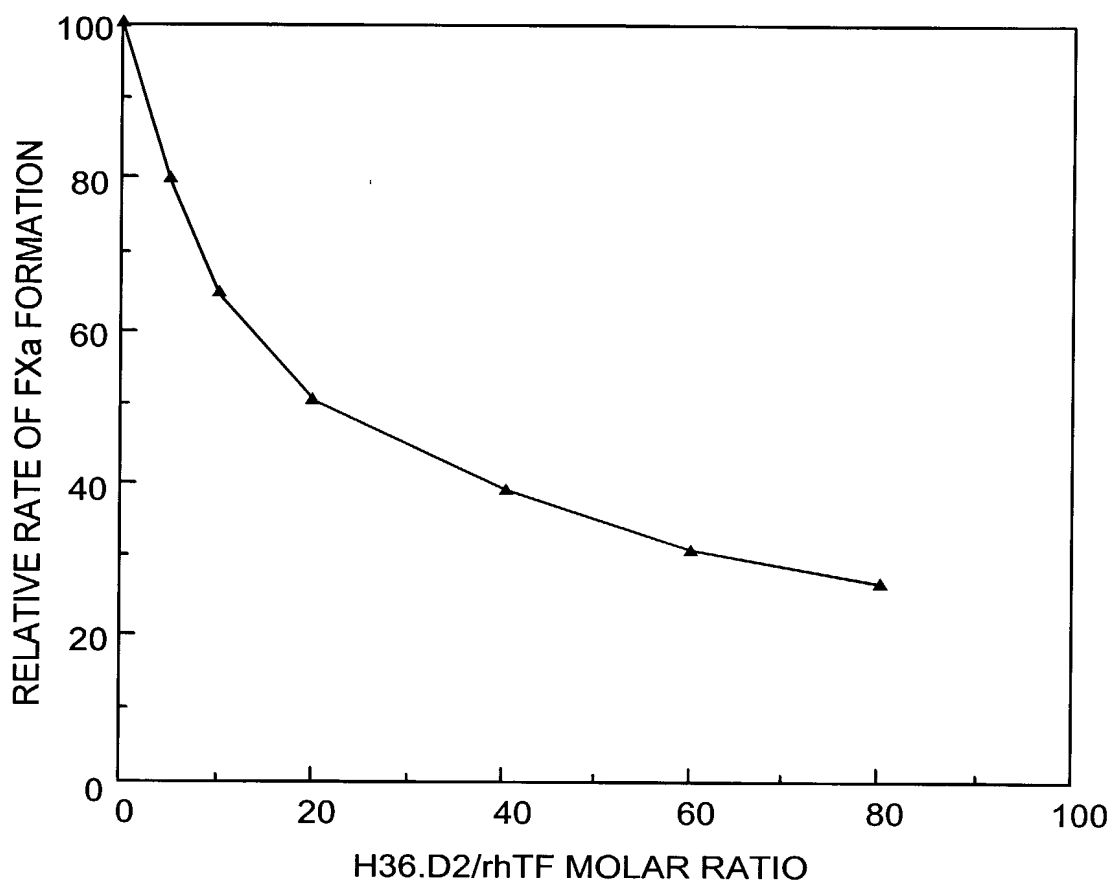


FIG. 6B

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H36.D2 CONCENTRATION (ng)	<u>% INHIBITION</u> CELLS (TF/FVII) AND H36.D2 PREINCUBATED PRIOR TO FX ADDITION	<u>% INHIBITION</u> FX AND H36.D2 ARE ADDED SIMULTANEOUSLY TO CELLS (TF/FVII)
0	0	0
50	88	nd
100	92	nd
200	97	nd
800	nd	76
1600	nd	78
3200	nd	92

FIG. 7

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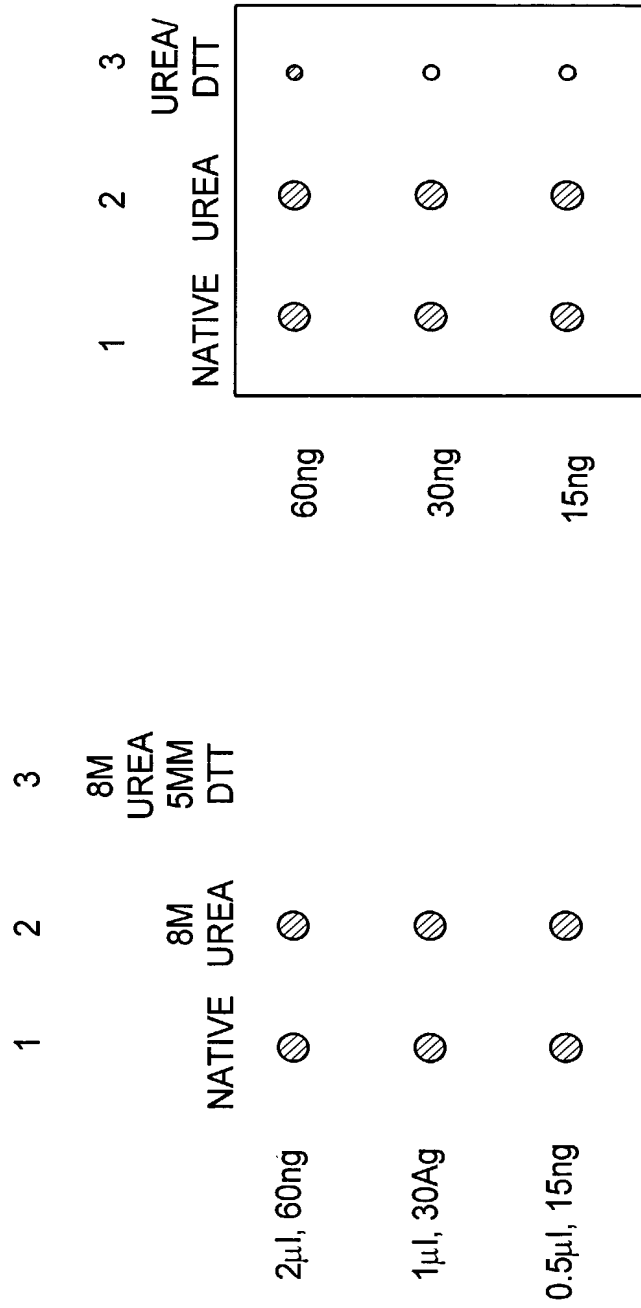


FIG. 8A

FIG. 8B

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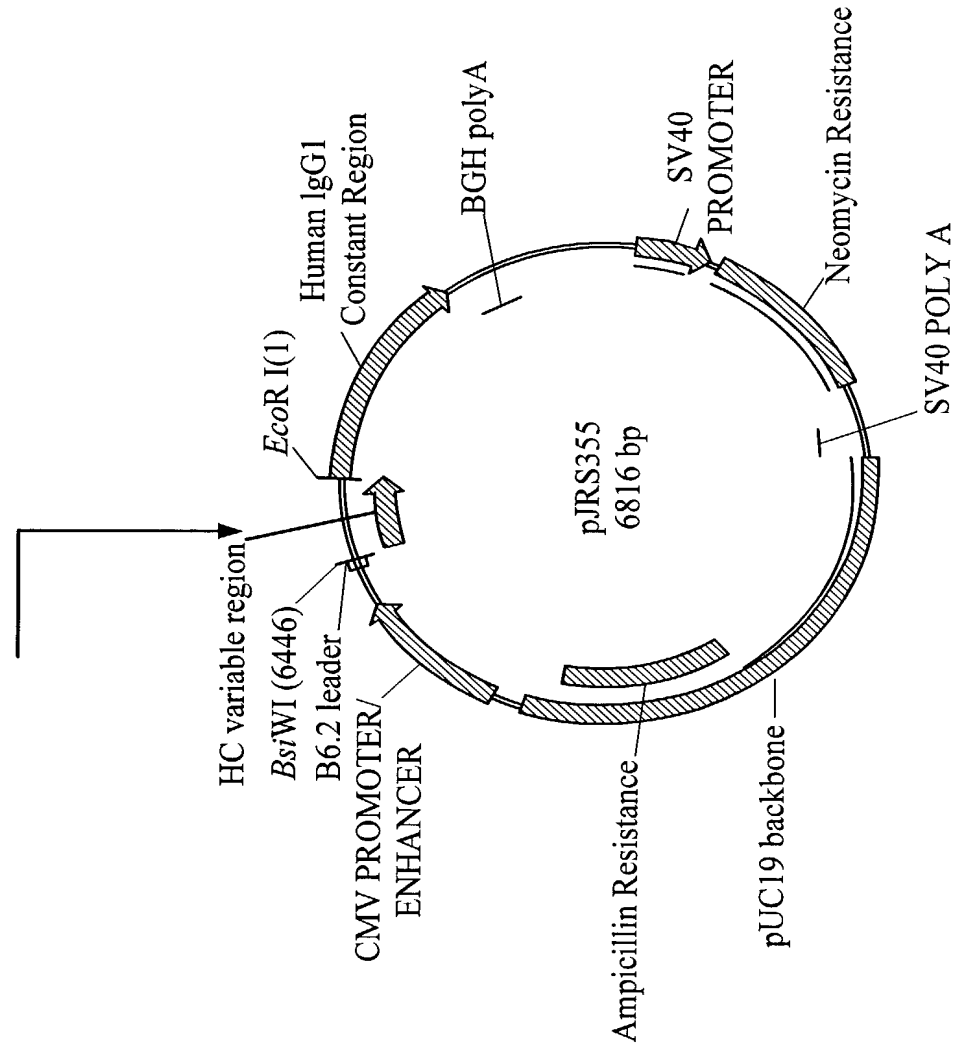


FIG. 9B

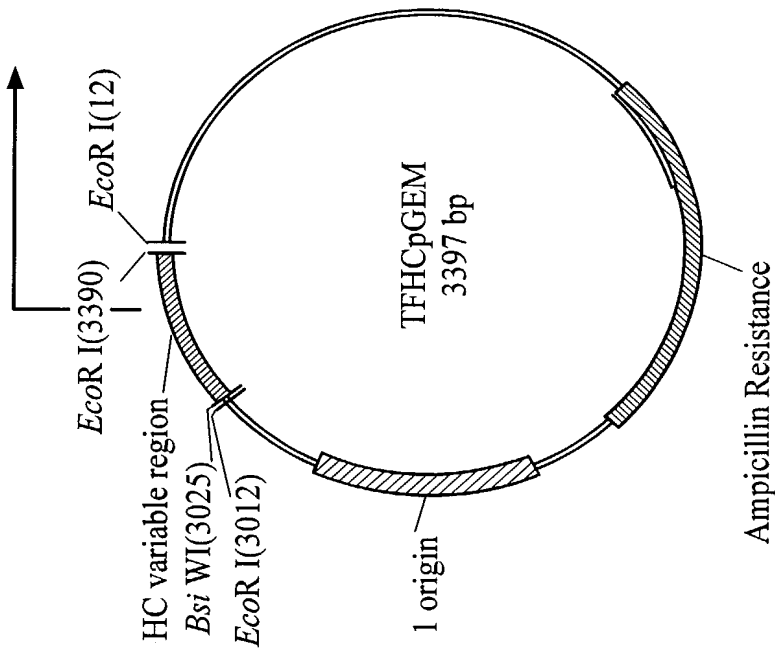


FIG. 9A

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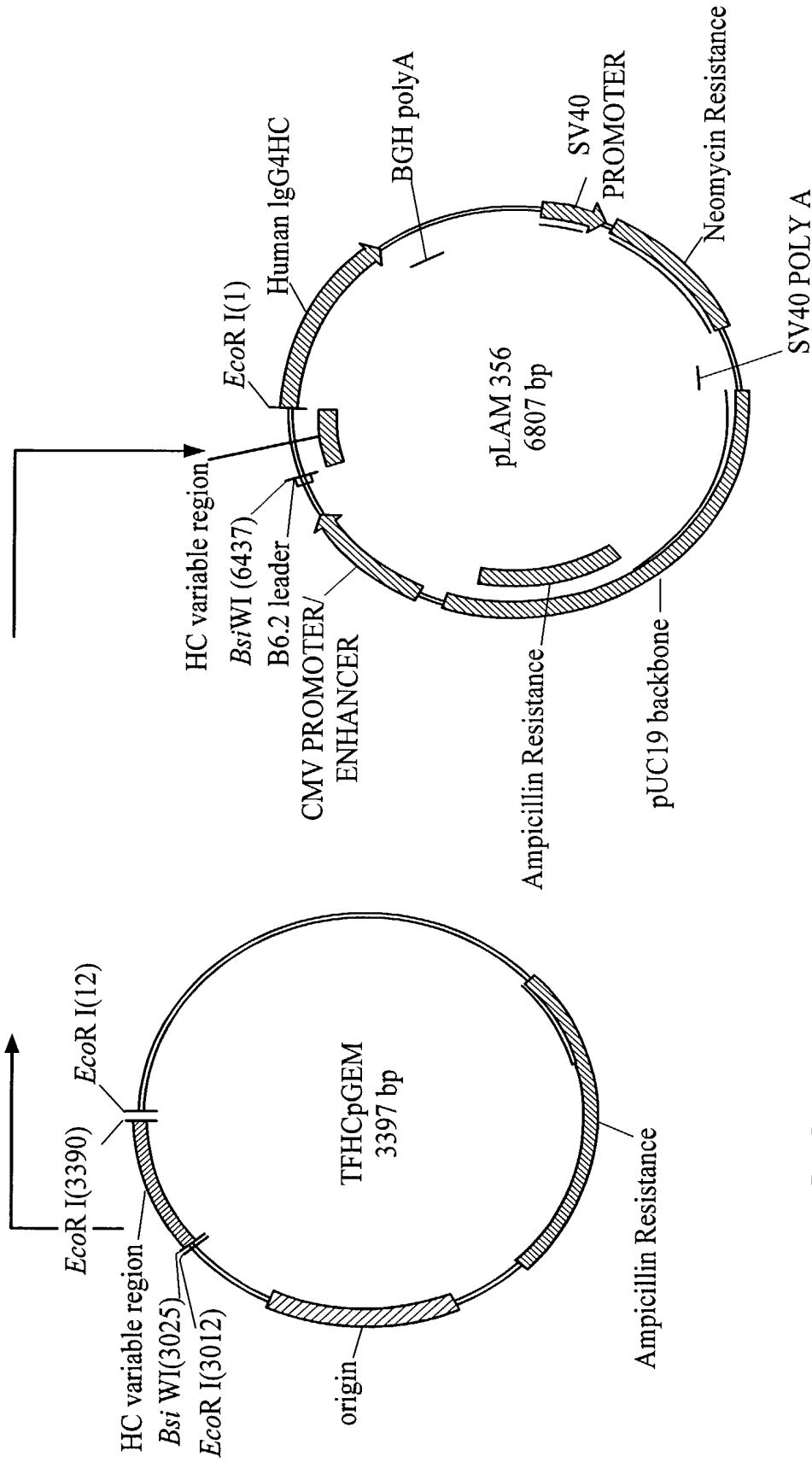


FIG. 9D

FIG. 9C

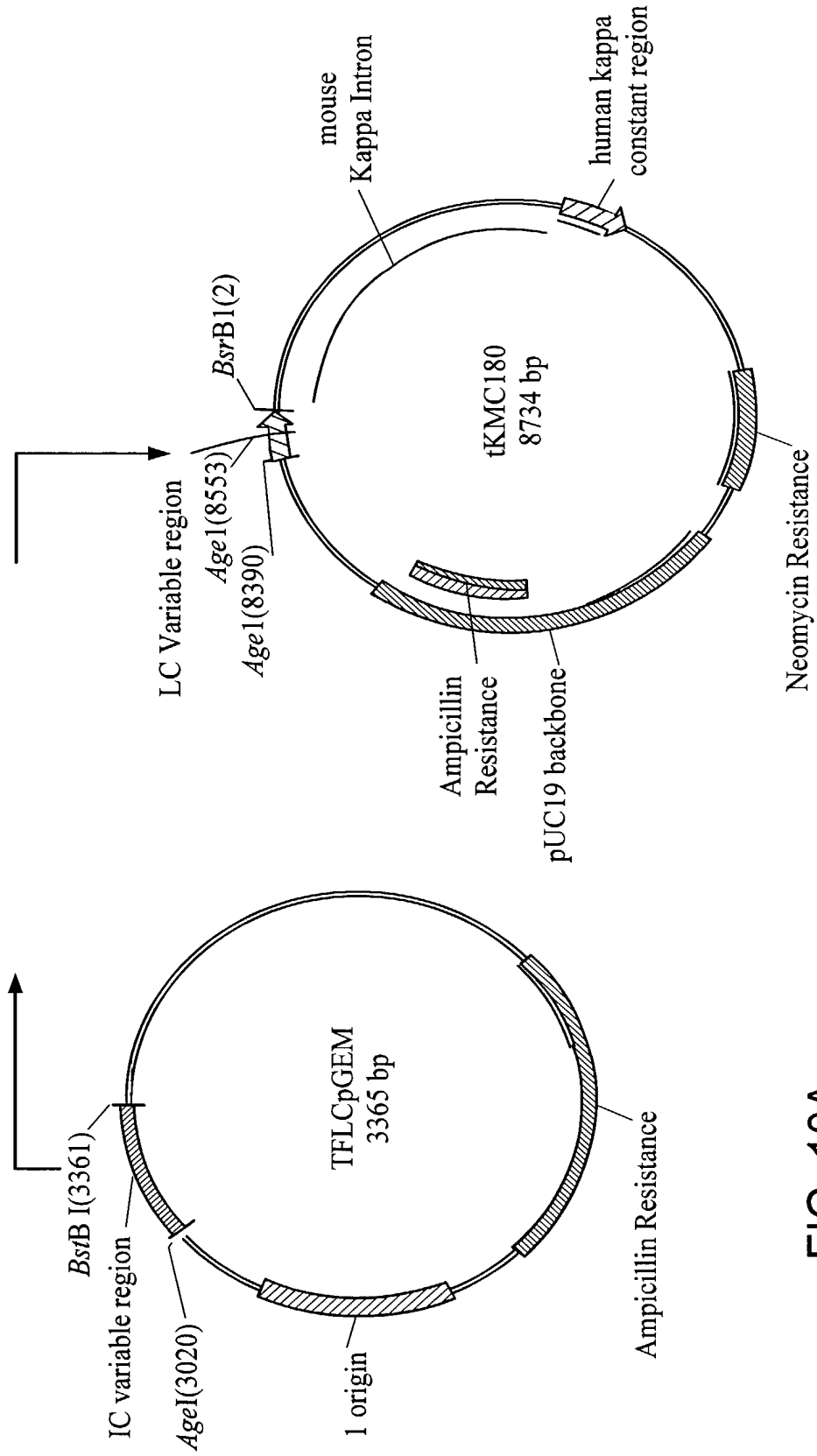


FIG. 10B

FIG. 10A

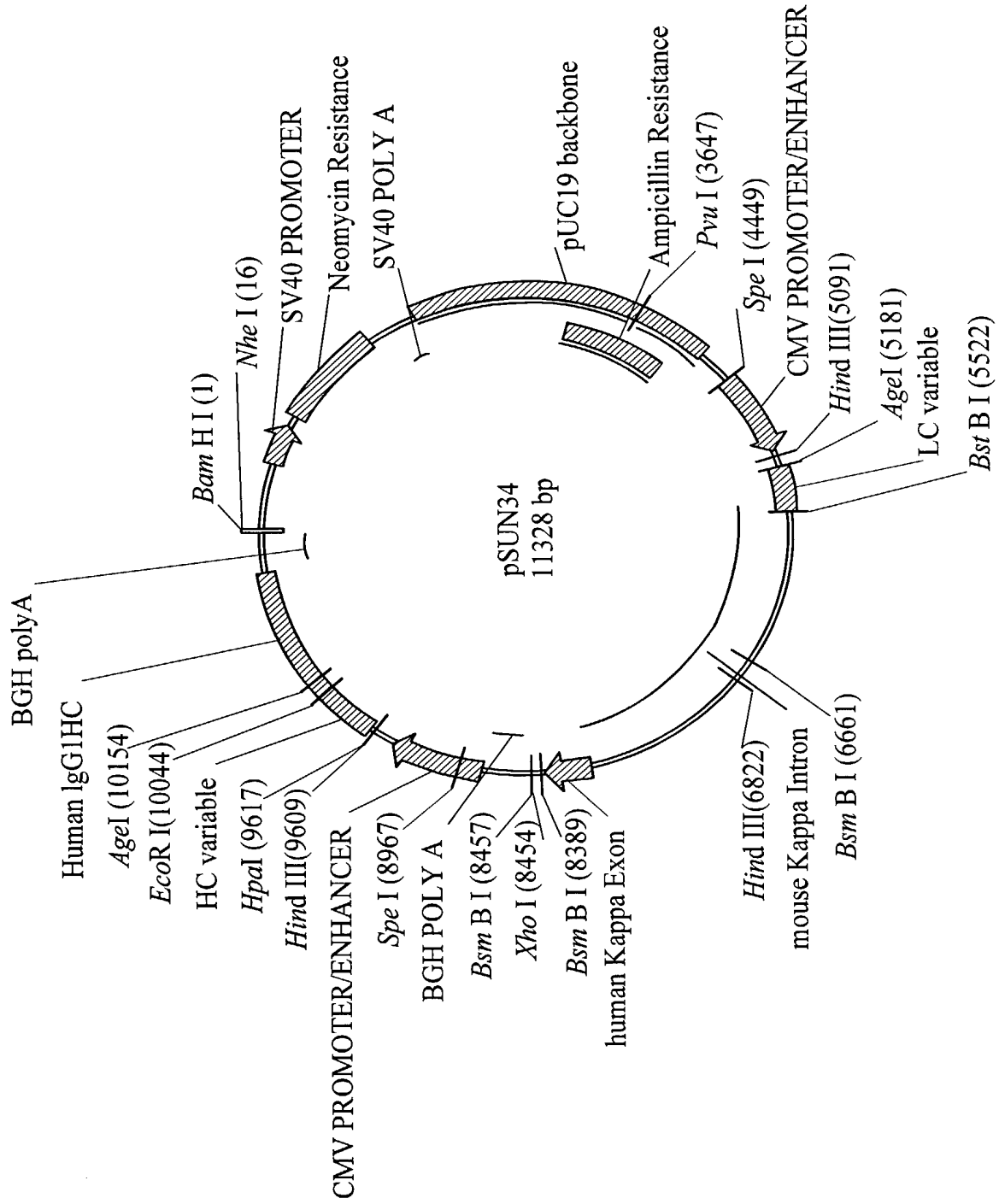


FIG. 11

Humanization of anti-Tissue Factor Antibody cH36

Sequences of Partially and Fully Humanized Light Chain (LC) Variable Regions

Light Chain (LC) FR Sequences										Names	
FR1 (23 AA)		FR2 (14 AA)			FR3 (32 AA)			FR4 (10 AA)			
1	10	20	35	47	57	60	70	80	86	98	107
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPSRFSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		cH36-LC	
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPSRFSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		LC-03	
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPS FSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		LC-04	
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPSRFSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		LC-05	
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPSRFSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		LC-06	
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPSRFSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		LC-07	
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPSRFSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		LC-08	
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPSRFSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		LC-09	
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPSRFSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		LC-10	
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPSRFSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		LC-11	
DIQMTQSPASQASLGESVTITC		WYQKPQKSPQLIY			GVPSRFSGSGSGTKFSFKISSLQAEDEVNYYC			FGAGTKLELK		LC-12	

FIG. 12A

Light Chain CDR Sequences of cH36

CDR1 (11 AA)		CDR2 (7 AA)		CDR3 (9 AA)	
24	34	50	56	89	97
L A S Q T I D T W L A		A A T N L A D		Q Q V Y S S P F T	

FIG. 12B

FIG. 12C

FIG. 12D

# Sequences of Partially and Fully Humanized Heavy Chain (LC) Variable Regions

## Heavy Chain (HC) FR Sequences

FR1 (30 AA)	FR2 (14 AA)	FR3 (32 AA)	FR4 (11 AA)	Names
1 10 20 29 36 44 67 75 85 95 107 117				
EIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSHGKSLEWIG	KATLTVDKSSTTAFMHLNLSLTSDSDSAVYFCAR	WGQGTTLTVSS	CH36-HC
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSHGKSLEWIG	KATLTVDKSSTTAFMHLNLSLTSDSDSAVYFCAR	WGQGTTLTVSS	HC-01
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAFMHLNLSLTSDSDSAVYFCAR	WGQGTTLTVSS	HC-02
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAFMHLNLSRSEDTA VYFCAR	WGQGTTLTVSS	HC-03
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAFMELSSLRSEDTA VYFCAR	WGQGTTLTVSS	HC-04
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAYMELSSLRSEDTA VYFCAR	WGQGTTLTVSS	HC-05
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAYMELSSLRSEDTA VYFCAR	WGQGTTLTVSS	HC-06
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAYMELSSLRSEDTA VYFCAR	WGQGTTLTVSS	HC-07
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAYMELSSLRSEDTA VYFCAR	WGQGTTLTVSS	HC-08
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAYMELSSLRSEDTA VYFCAR	WGQGTTLTVSS	HC-08R1
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAYMELSSLRSEDTA VYFCAR	WGQGTTLTVSS	HC-11
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAYMELSSLRSEDTA VYFCAR	WGQGTTLTVSS	HC-12
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAYMELSSLRSEDTA VYFCAR	WGQGTTLTVSS	HC-09
QIQLOQSGPELVKPGASVQVSCKTSGYSFT	WVRQSPGKGLEWIG	KATLTVDKSSTTAYMELSSLRSEDTA VYFCAR	WGQGTTLTVSS	HC-10

FIG. 13A

## Heavy Chain CDR Sequences

CDR1 (5 AA)	CDR2 (17 AA)	CDR3 (8AA)	Names
31 35	50 66	99 106	CH36
D Y N V Y	Y I D P Y N G I T I Y D Q N F K G	D V T T A L D F	
31 35	50 66	99 106	HC-08
D Y N V Y	Y I D P Y N G I T I Y D O N L K G	D V T T A L D F	

**FIG. 13B**

FIG. 13D



